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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/809,329	03/16/2001	Marie Christine Bissery	03806.0493	5359

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EXAMINER
HENRY, MICHAEL C

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 02/05/2003

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/809,329	BISSERY, MARIE CHRISTINE	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/13/2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 11/13/02.

The amendment filed, 11/13/02 affect the application, 09/623,495 as follows:

1. Claims 1, 2, 11 and 13 have been amended. This leaves Claims 1-20.
2. Applicant responds to the rejection under 35 USC 102(b) by amending claims 1,2,11and 13.
3. The responsive to applicants' arguments is contained herein below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Furuta et al. (Jpn J Cancer Chemother 18 (3): 393-402, 1991).

In claim 1, applicants claim "a synergistic therapeutic pharmaceutical composition for solid tumors comprising an effective amount of camptothecin, or a camptothecin derivative, in combination with an effective amount of a topoisomerase II inhibitor, wherein said composition provides a synergistic effect in the treatment of solid tumors."

Furuta et al. disclose applicant's claimed, therapeutic pharmaceutical composition, comprising an effective amount of camptothecin derivative (CPT-II), in combination with an effective amount of a topoisomerase II inhibitor (adriamycin or doxorubicin), wherein said composition provides a synergistic effect in the treatment of tumors (see summary or abstract and tables). The applicant's composition of

claims 2-7, 9-12 is also anticipated by Furuta et al. (see summary or abstract and tables). It should be noted that claims 1-7, 9-11 are composition claims and the recitation of the intended utility of the composition is not a further limitation of the claim. The examiner gives very little weight to said intended utility.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5,8,13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuta et al.

In claims 5 and 7, applicant claims a composition as in claim 3 and 6 respectively, wherein said antibiotic is daunomycin (claim 5) and wherein said epipodophyllotoxin is teniposide (claim 7).

Furuta et al. disclose a composition as in claim 3 and 6 respectively, wherein said antibiotic is adriamycin and wherein said epipodophyllotoxin is etoposide.

The difference between applicant's claimed method and the method taught by Furuta et al. is that the applicant's antibiotic is daunomycin as compared to adriamycin and applicant's epipdophyllotoxin is teniposide as compared to etoposide. However, daunomycin and adriamycin are both well known anthracycline antibiotics or antitumor agents of very similar structure. That is, they can be considered species of the same genus. Also, the

epipdophyllotoxin, teniposide and etoposide are antitumor agents that can also be considered species of the same genus.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Furuta et al., to prepare and administer a therapeutic pharmaceutical composition, comprising an effective amount of camptothecin, or a camptothecin derivative, in combination with an effective amount of a topoisomerase II inhibitor like daunomycin (which can be considered to belong to the same genus as adriamycin (doxorubicin), for the treatment of different tumors.

One having ordinary skill in the art would have been motivated in view of Furuta et al., to prepare and administer a therapeutic pharmaceutical composition, comprising an effective amount of camptothecin, or a camptothecin derivative, in combination with an effective amount of a topoisomerase II inhibitor like daunomycin based on need, like the type and/or degree of severity of the tumor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuta et al.

In claim 13, applicant claims a method of treating a solid tumor, comprising administering an effective amount of camptothecin, or a camptothecin derivative, as a first agent, in combination with administration of an effective amount of a topoisomerase II inhibitor as a

second agent, wherein the agents are administered simultaneously, semi-simultaneously, or separately.

Furuta et al. disclose a method of treating a tumor (L 1210 leukemia), comprising administering an effective amount of a camptothecin derivative, as a first agent, in combination with administration of an effective amount of a topoisomerase II inhibitor as a second agent, wherein the agents are administered simultaneously, semi-simultaneously, or separately (see abstract and tables).

The difference between applicant's claimed method and the method taught by Furuta et al. is that the applicant's type of tumor that is treated.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Furuta et al., to use the method of Furuta et al. to treat various types of tumors like solid tumors, and to use antitumor agents taught by Furuta et al. that belong to the same genus as (adriamycin and daunomycin) and (teniposide and etoposide) for the treatment of different tumors, based on need, like the type and/or degree of severity of the tumor.

One having ordinary skill in the art would have been motivated in view of Furuta et al., to use the method of Furuta et al. to treat various types of tumors like solid tumors, and to use antitumor agents taught by Furuta et al. that belong to the same genus as (adriamycin and daunomycin) and (teniposide and etoposide), for the treatment of different tumors, based on need, like the type and/or degree of severity of the tumor.

It should be noted that claims 14-20 are also obvious in view of Furuta et al., and that the oral administration of the composition as recited in claim 20 is also based on need, like the type and/or degree of severity of the tumor and the subject that is treated.

Response to Amendment

Applicant's arguments filed November 13, 2002 have been fully considered but they are not persuasive.

The applicant argues that "although Furuta et al. states that the treatment with CPT-11 and adriamycin (i.e., doxorubicin) provides synergistic effects, this reference does not, in fact, disclose or suggest a synergistic combination according to the present invention. The present application, at page 5, second full paragraph, defines a synergistic combination of two constituents as one that provides a therapeutic effect that is superior to one or the other constituent of the combination when used at its optimum dose (i.e., highest non-toxic dose). Thus, according to the present invention, the maximum tolerated dose of each individual constituent is determined, and a combination having a superior therapeutic effect is developed based on the maximums identified for each individually." However, the definition of synergism (or synergistic effects) is not limited to the applicant's condition or term that he/she refers to as optimum dose (i.e., highest non-toxic dose). In fact, Webster's New World Dictionary (3rd college edition, 1988, page 1358) defines synergism as "the simultaneous action of separate agencies which, together, have greater total effect than the sum of their individual effects; said esp. of drugs ...." Yet another definition states that "it is not uncommon for the effect of two chemicals on an organism to be greater than the effect of each chemical individually, or the sum of the individual effects. The presence of one chemical enhances the effects of the second. This is called a synergistic effect or synergy, and the chemicals are sometimes described as showing synergism." (see, http://physchem.ox.ac.uk/MSDS/glossary/synergistic_effect.html, The Physical and Theoretical Chemistry Laboratory,Oxford University, England Chemical Safety

Information - Glossary). Based on the aforementioned definitions, synergism is not limited to an optimum dose (i.e., highest non-toxic dose) and therefore, Furuta et al. do not have to disclose an optimum dose (i.e., highest non-toxic dose) in reporting synergism or synergistic effects of their composition. Also, Furuta et al. data of Table 3 shows that the effect (survival times) of two chemicals (CPT-II and adriamycin) on the inoculated mice (an organism) is greater than the effect of each of these chemicals individually (for example, 12.5 mg/kg of CPT-II + 6.25 mg/kg of adriamycin produces a survival time of 16.5 ± 1.7 days whereas, 12.5 mg/kg of CPT-II produces a survival time of 10.8 ± 0.4 days and 6.25 mg/kg of adriamycin produces a survival time of 11.7 ± 0.7 days; based on three administrations (days 1,5,9) per dosing regimen). This result complies with the latter stated definition of synergism or synergistic effect and also with applicant's definition excluding the limitation or term, "when used at maximum dose". Moreover, applicant's synergistic therapeutic pharmaceutical composition, as claimed reads on Furuta et al.' synergistic therapeutic pharmaceutical composition.

The Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 703 308-7307. The examiner can normally be reached on 8:30 am to 5:00 pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703 308-4624. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-1235.

MCH

January 22, 2003

SAMUEL BARTS
PRIMARY EXAMINER
GROUP 1600